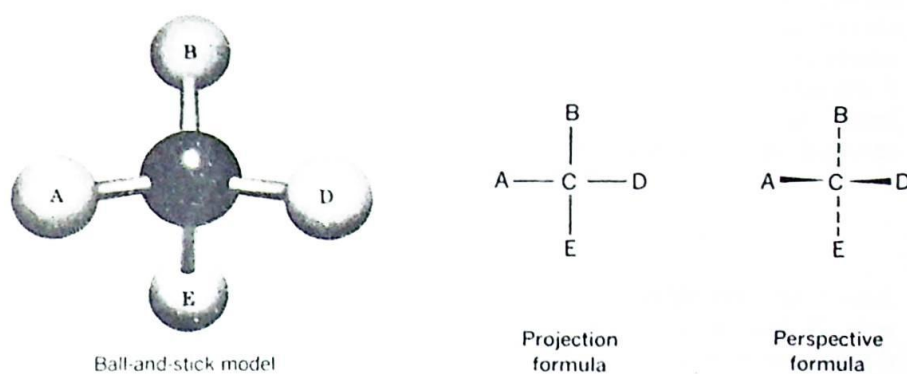
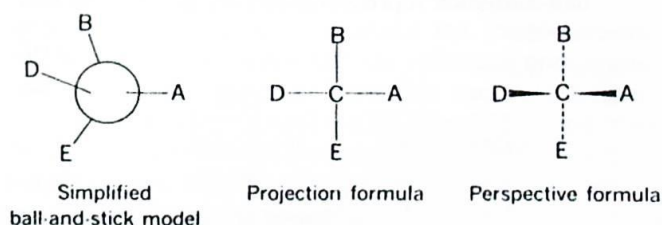


possible isomers. One way of representing them is to use the **projection formula** introduced in the nineteenth century by the illustrious German organic chemist, Emil Fischer. The projection formula represents the four groups attached to the carbon atom as being projected onto a plane. This projection can be represented for the asymmetric molecule depicted previously as shown in Structure 2.4. In the Fischer



STRUCTURE 2.4

projection formula, the horizontal bonds are understood to be in front of the plane of the paper, while the vertical bonds are behind. This relationship is seen more clearly in the **perspective formula**. Here, dashed lines indicate bonds extending behind the plane of the page, while solid wedges identify bonds projecting forward out of the plane of the page. The projection and perspective formulas can be used to distinguish between the compound shown in Structure 2.4 and its mirror isomer below. These two pairs of formulas together with a **simplified version** of the ball-and-stick model constitute three different ways of writing formulas to represent the enantiomeric pairs.

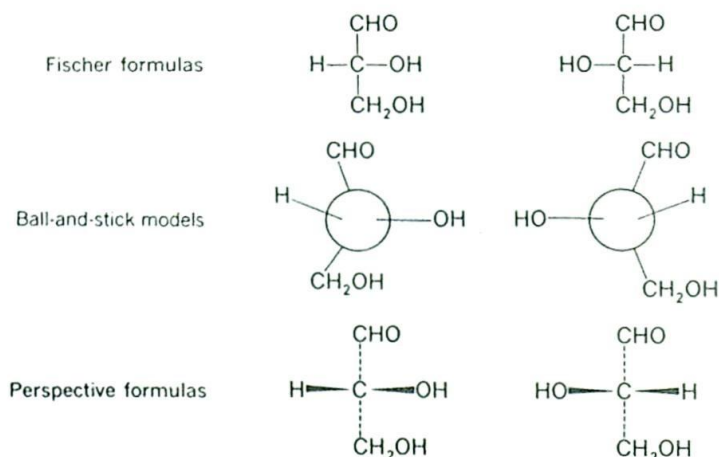


In one's imagination, the perspective formula can be rotated in all planes without fear of confusing the two enantiomers. Caution is required in the use of the Fischer formulas; although they may be rotated a full 180° in the plane of the paper, rotation of only 90° results in the enantiomer because of the convention that the horizontal bonds are represented as being in front of the plane of the paper. The Fischer formula cannot, in the mind's eye, be removed from the plane of the paper.

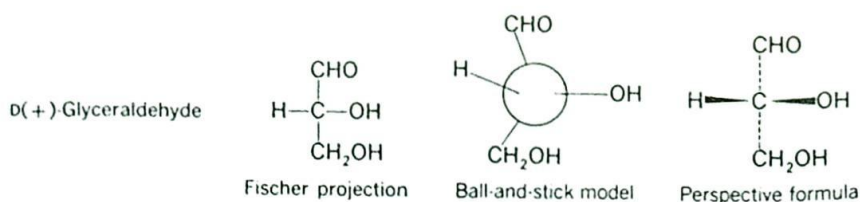
2.2.4 D-GLYCERALDEHYDE AS A REFERENCE COMPOUND

With the existence of a large number of optical isomers in carbohydrates, it is also necessary to have a reference compound. The simplest monosaccharide

that possesses an asymmetric carbon atom has been chosen as the reference standard; this compound is the triose **glycerose** or **glyceraldehyde**. Since this compound has a chiral center, it can exist as two stereoisomers. These may be represented by their Fischer projection formulas as well as the simplified ball-and-stick models and perspective formulas.



These three pairs of structures are related to each other as mirror image isomers. Although they will have the same melting point, boiling point, and solubility in H_2O , they will differ in the direction in which they rotate plane-polarized light. The isomer that rotates light in the clockwise direction is identified with the symbol (+) to indicate that it is the dextrorotatory enantiomer. At the turn of this century, that isomer was also assigned the Fischer formula in which the hydroxyl group appears on the right when the aldehyde group is at the top. Moreover, it was agreed that this form should be designated as **D(+)-glyceraldehyde**. For clarification, both the projection formula and the frequently seen ball-and-stick representations are given.



This assignment of the above structures to the glyceraldehyde isomer that rotated polarized light in the clockwise direction had only a 50:50 chance of being correct. Fifty years later, research involving x-ray diffraction studies on tartaric acid showed that Fischer's choice was the correct one.

D(+)-Glyceraldehyde serves an important role as a reference compound not only for carbohydrates, but also for hydroxy and amino acids encountered in biochemistry. The **D** and **L** notation has been particularly useful in relating groups of carbohydrates (the naturally occurring **D**-sugars) and amino acids (the naturally occurring **L**-amino acids). However, the **D** and **L** system cannot be used for all compounds containing chiral centers, since, in theory, this would call for converting the compound of interest into **D**- or **L**-glyceraldehyde or a

compound known to be related by stereochemistry to these reference standards. Therefore, a new system called the Cahn–Ingold–Prelog “sequence rule” has been devised to describe, in an absolute manner, the configuration of individual chiral centers. In brief, the method is based on orienting the molecule so that the smallest ranked group attached to the chiral center is facing away and then observing the direction, clockwise (*R* for *rectus*) or counterclockwise (*S* for *sinister*), that one’s eye takes as it moves in an assigned **order of rank** from the highest atomic number of the substituent atoms to the lowest. According to the sequence rule, *D*(+)-glyceraldehyde would be designated as (*R*)-glyceraldehyde. Although the sequence rule is employed in many areas of organic chemistry, it is not convenient to use with carbohydrates or amino acids for which the “local systems” based on *D*(+)-glyceraldehyde and *L*_α-serine are retained (see Sections 2.2.5 and 4.2).

2.2.5 CYANOHYDRIN SYNTHESIS

As an illustration of the use of *D*-glyceraldehyde as a reference compound, consider the formation of tetrose sugars from a triose by the **Kiliani–Fischer** synthesis. This synthesis is a process by which the chain length of an aldose is increased by one carbon atom, and two new aldoses are formed (Figure 2.1). In this synthesis, the chirality of the asymmetric carbon in *D*-glyceraldehyde is not disturbed, but the aldehyde carbon is converted into a new chiral center. Therefore, two four-carbon compounds with opposite configuration at that center are formed. These new compounds are *D*-erythrose and *D*-threose; the *D*-prefix specifically denotes their relationship to *D*-glyceraldehyde. If the cyanohydrin synthesis were applied to *L*-glyceraldehyde, *L*-erythrose and *L*-threose would be formed.

When the Kiliani–Fischer synthesis is applied to the two *D*-aldotetroses shown in Figure 2-1, four aldopentoses are formed. Elongation of these four pentoses results in a total of eight aldohexoses including the familiar *D*-glucose, *D*-mannose, and *D*-galactose.

At this point, it is informative to consider the stereochemical relationships between the eight aldohexoses and the reference compound *D*-glyceraldehyde. First, the eight hexoses have the same structural formula, $\text{CH}_2\text{OH}-\text{CHOH}-\text{CHOH}-\text{CHOH}-\text{CHOH}-\text{CHO}$ and therefore are stereoisomers rather than structural isomers. Second, with regard to their stereoisomerism, they are optical rather than geometric isomers. Third, these *D*-aldohexoses are structurally related to *D*-glyceraldehyde because in theory they could all have been produced by application of the cyanohydrin synthesis to that triose. This relationship is also shown in the projection formulas for the eight hexoses in which the hydroxyl ($-\text{OH}$) group on the **reference carbon atom**, the highest-numbered chiral carbon, is on the right as in *D*-glyceraldehyde (the carbons in aldoses are numbered starting with the aldehyde carbon). Fourth, these aldohexoses are related to each other as diastereoisomers; they cannot be enantiomeric since their mirror-image isomers, for example, *L*-glucose, the mirror image of *D*-glucose, is not shown. Fifth, four pairs of **epimers**, diastereomers differing in the configuration at a **single carbon atom**, exist among the aldohexoses (e.g., *D*-allose and *D*-altrose). Finally, the fact that these sugars are all “*D*-sugars” derived from *D*-glyceraldehyde bears no relationship to whether the sugar is dextrorotatory or levorotatory.

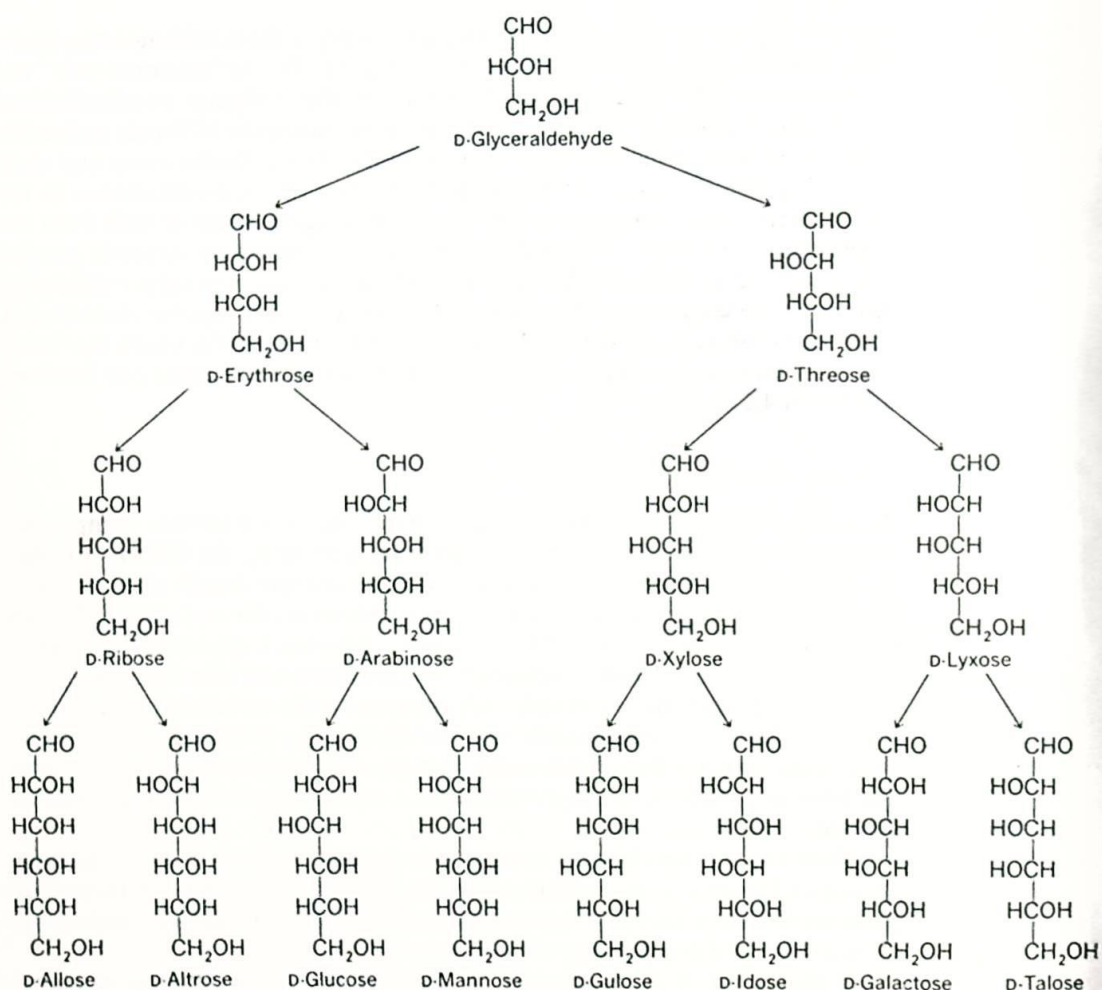


FIGURE 2.1 Structures of the D-aldoses.

As the number of asymmetric carbon atoms increases in a carbohydrate molecule, the number of optical isomers also increases. Van't Hoff established that 2^n represents the number of possible optical isomers, where n is the number of asymmetric carbon atoms. Thus, in the trioses where n is 1, there are two optical isomers; in the tetroses where n is 2, four optical isomers, known as D-erythrose, L-erythrose, D-threose, and L-threose, occur. In the aldohexoses, where there are four asymmetric carbon atoms, there are 16 optical isomers, eight of which are the D-sugars shown in Figure 2.1. In the ketohexoses, when n is 3, there are eight possible isomers.

Although Figure 2.1 shows eight aldohexoses, only three of these are frequently encountered in nature. Their projection formulas are repeated here together with the structure of D-fructose, an important ketohexose. The following statements can be made about